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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/083,476	02/27/2002	Roger N. Piasio		4777

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 07/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,476	PIASIO ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/30/04 & 1/2/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election

1) Acknowledgment is made of Applicants' election filed 10/01/03 in response to the restriction requirement mailed 03/30/04. Applicants have elected invention I, claims 1-8, with traverse. Applicants allege that claim 9 is not shown to be patentably distinct from the subject matter claimed in claims 1-8. Applicants state that the restriction requirement arbitrarily states that the method steps/ parameters are distinct from one another and that the reagents or materials are different. Applicants contend that the single method step in each instance consists of allowing sample to flow along a preprepared ICT test strip to a 'capture' zone containing predeposited labeled antibodies, allowing the sample and test strip to rest for about 15-20 minutes and observing the result. Applicants admit that the difference between invention I and invention II consists in the preliminary preparation of the ICT test strip in that in invention I, the concentration of labeled antibody immovably fixed at the capture line of the strip is reduced, whereas in invention II, the concentration of labeled antibodies at the capture line retains its original concentration. Applicants characterize the two inventions to include two variants of ICT test strip preparations. Applicants submit that both inventions have the object of distinguishing samples obtained from healthy but colonized patients thereby avoiding false positive tests and inadvertent medication of healthy patients. Applicants state that the subject matter is not divergent; it involves the same reagents and the same field of search; and only the concentrations of reagents are varied. Applicants assert that insofar as the end user of the test is concerned, it is performed identically regardless of how the test is prepared.

Via the election filed 04/30/04 in response to the election of species requirement mailed 03/30/04, Applicants have elected the antigen species characteristic of *Streptococcus pneumoniae*. Since Applicants did not distinctly and specifically point out the supposed errors in the election of species requirement, the election has been treated as an election without traverse (M.P.E.P § 818.03(a)).

Applicants' arguments have been carefully considered. Upon further consideration, the currently non-elected claim 9 is categorized as being drawn to the second improvement species as opposed to the second invention. Accordingly, claim 9 would be retained as a pending claim being drawn to a non-elected species.

Status of Claims

2) Claims 1-9 are pending.

Claims 1-8 have been elected.

Claim 9 has been withdrawn from consideration as being directed to a non-elected species.

Claims 1-8 are under examination. A First Action on the Merits for these claims is issued.

Specification

3) The instant specification is objected to for reciting co-pending application(s) which itself incorporates essential material by reference. The co-pending application, 09/518,165, recited repeatedly in the instant specification, itself incorporates essential material by reference, to other co-pending applications, such as, 09/139,720; 09/458,988 etc. MPEP requires that in any application which is to issue as a U.S. patent, essential material may not be incorporated by reference to a U.S. patent application which itself incorporates essential material by reference.

Rejection(s) under 35 U.S.C. § 112, First Paragraph

4) The following is a quotation of the first paragraph of 35 U.S.C § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5) Claims 1-8 are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant claims are evaluated based on *Wands* factors. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

The instant specification indicates that the instantly claimed invention is obtained by modifying the ICT NOW® bioassay. The state of the art reflects unpredictability and lack of success with Binax

NOW bioassay for serologically distinguishing children with pneumococcal pneumonia from those who are merely colonized. For instance, see abstract of Dowell *et al.* (*Clin. Infect. Dis.* 32: 824-825, 2001). Dowell *et al.* taught that the test was significantly more likely to be positive among children who were nasopharyngeal carriers of pneumococci (see abstract; Table 1; and page 824). More than half of the patients who did not have pneumonia but who had pneumococci in their nasopharynx had a positive result of the urine antigen detection test (see paragraph bridging 824 and 825). Similarly, Adegbola *et al.* (*Pediatr. Infect. Dis. J.* 20: 718-719, July 2001) stated the following with regard to the use of Binax NOW test (see page 719):

> ..... The detection of urinary antigen in more than one-half of the children colonized by *S. pneumoniae* indicates that a positive result from this test does not necessarily imply active disease in children. Thus when used in a community with high pneumococcal carriage, a positive result from Binax NOW test must be interpreted with caution. The two "false positive" tests in our study may indeed have been true positives because the presence of pneumococcal antigen resulting from colonization is intermittent and pneumococcal antigen could be excreted in urine after the disappearance of *S. pneumoniae* from the nasopharynx.
>
> ..... Binax NOW test would likely be of limited value for detection of childhood pneumococcal pneumonia in our study population. In a recent study of the etiology of pneumonia in Beijing, China, the Binax NOW test was no more likely to be positive among children with radiographically confirmed pneumonia than among control children, and it was more likely to be positive among children who were colonized by *S. pneumoniae*. The test my also be of limited value in the diagnosis of adult pneumonia because of the relatively high carriage rates of *S.* pneumoniae in Gambian adults. ..... There was no correlation between the magnitude of nasopharyngeal carriage and the intensity of the color line in positive tests.

The above-cited facts being reflective of the state of the art, one of skill in the art would look into Applicants' specification for clear, complete and precise direction and guidance to practice the invention as claimed. A review of the specification indicates the following. The specification repeatedly keeps referring to the disclosure of a 'commonly assigned' co-pending application, 09/399,710. For example, the 'Detailed Description of the Invention' on pages 7 and 10 of the specification refer to a co-pending US patent application, 09/399,710. The sentence bridging pages 7 and 8 of the specification states the following:

> The modification disclosed herein of the NOW® test disclosed and claimed in U.S. Serial No. 09/399,710 render the test as so modified highly useful in enabling physicians to make rapid, accurate diagnosis of pneumococcal pneumonia and/or otitis media caused by *Streptococcus pneumoniae* in children, which diagnoses are based on the modified test results combined with clinical observations of the individual patients.

The specification further refers to another co-pending application, 09/518,165. The first full sentence on page 8 of the specification states the following:

> Analogous modifications of the tests covered in U.S. Serial No. 09/518,165 render those tests as so modified very useful in enabling physicians to make rapid, accurate diagnoses of pneumonic diseases and otitis media of

> other bacterial origin in children, by combining the modified test results with clinical observation of individual child patients.

The second full paragraph on page 5 of the specification states as follows:

> Copending, commonly assigned U.S. application Serial No. 09/518,165 filed March 1, 2002, describes and claims rapid immunochromatographic tests for detecting bacterial carbohydrate antigens in human bodily fluids, including urine.

Neither of these co-pending applications have been incorporated by reference into the specification at the time of filing. The instant application is not related to these 'commonly assigned' co-pending applications in terms of priority or continuity. Page 8 of the instant specification states that 'a brief summary of the bioassay format described in both of the prior co-pending applications is provided'. The co-pending applications are stated to provide a purification process for an essentially protein-free carbohydrate antigen characteristic of the bacteria. Paragraph bridging pages 8 and 9 of the specification provides a brief description of the disclosure of the co-pending applications. This brief description, however, is insufficient for one of skill in the art to practice the instant invention as claimed. The first sentence in the last paragraph on page 10 of the specification states the following:

> In all of these Examples, test strips were prepared as described in earlier filed, copending Serial No. Application 09/399,710 using antibodies to *Streptococcus pneumoniae* that has been purified and rendered antigen-specific as described in that application.

The patent application 09/399,710, now issued as US patent 6,409,683, does not appear to be commonly assigned. The US patent 6,409,683 is entitled 'Medical guidewire with improved coil attachment' and appears to have nothing in common with the instant application or invention. No test strips using antibodies to *Streptococcus pneumoniae* that had been purified and rendered antigen-specific are disclosed or described in the patent application 09/399,710. The disclosure of the application 09/399,710, does not provide enablement for the instantly claimed invention. The other co-pending U.S. patent application cited by Applicants in the instant specification, 09/518,165, appears to disclose subject matter relevant to the instantly claimed invention. The claims of the co-pending application 09/518,165 however stand rejected currently due to the lack of an enabling disclosure. In order to make the required modifications to the tests described in the examples of the instant application, i.e., to practice the instant invention, one has to know of the bioassay format described in the recited two patent applications, 09/399,710 (US 6,409,683) and 09/518,165. MPEP requires that an application as filed must be complete in itself in order to comply with 35 U.S.C. § 112. The disclosure of the patent application SN 09/399,710, even if it was incorporated by reference at the time of original

filing, does not provide disclosure on the bioassay format, such that it can be modified as described in the examples of the instant application, to produce the instantly claimed invention. In other words, modification of what is described in the patent application, 09/399,710, does not result in the improvement claimed in the instant claims. The co-pending application, 09/518,165, has not been incorporated by reference into the instant application at the time of filing. Furthermore, the application 09/518,165 itself incorporates essential material by reference, to other co-pending applications, such as, 09/139,720; 09/458,988 etc. MPEP requires that in any application which is to issue as a U.S. patent, essential material may not be incorporated by reference to a U.S. patent application which itself incorporates essential material by reference.

It is important that the essential material that renders the claimed invention novel must be described in the instant specification in full detail such that one of skill in the art can practice the invention without undue experimentation. Specific operative embodiments must be precisely and fully described. An incomplete disclosure or description does not enable one of skill in the art to which the invention pertains to make and use the invention as of its effective filing date.

Furthermore, the instant claim 1 is very broad. The term 'antigen' encompasses a protein antigen, a peptide antigen, a lipid antigen, a glycolipid antigen, a glycoprotein antigen, a carbohydrate antigen, a neoantigen etc. The antigen can be isolated or non-isolated being present on the surface of the whole bacteria. The recited bacteria encompass aerobic and anaerobic bacteria as well as Gram positive and Gram negative bacteria. In order to use 'antibodies to said antigen' in each generic bioassay, one has to produce antibodies to the antigen that is characteristic of any of these bacteria. The claimed bioassay improvement is applicable for detection of any bacterial agent causative of human ear and respiratory tract infections, including those yet to be discovered, which also colonize the nasopharynx areas of children of the recited age. An unpurified antigen of such bacteria is unlikely to yield antibodies that would provide the bioassay specificity of 90%, and no or substantially reduced incidence false positive results stemming from nasopharyngeal colonization of otherwise healthy children. The method for obtaining antigen-specific antibodies to target bacterial antigens claimed in the recited co-pending application, 09/518,165, i.e., a part of essential material needed for practicing the instant invention, stand rejected based on lack of an enabling disclosure.

Clearly, undue experimentation would have been required by one of skill in the art at the time of the invention due to the lack of direction and specific guidance, the lack of enabling disclosure, the

unpredictability and lack of success as indicated by the state of the art, and the quantity of experimentation necessary.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

6) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

7) Claims 1-8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant(s) regards as the invention.

(a) Claim 1 is indefinite and confusing. Line 1 of claim 1 recites that the bioassay is 'for the detection in bodily fluids of teenage and adult humans' of the recited antigen. Lines 5 and 6 of the claim state that 'the improvement in said bioassay for detection of said antigen in bodily fluid samples from said children up to the age of about 12 years which at least substantially reduces the incidence of false positive results stemming from nasopharyngeal colonization of otherwise healthy children'. The last few lines of claim 1 state that 'the tests representing each variation are run identically on samples of bodily fluids taken from each of (1) otherwise healthy children known to have nasopharyngeal colonization by the bacteria; and (2) children known to have an ear or pneumococcal infection. It is unclear whether the improvement in the bioassay is for detecting the recited antigen in bodily fluids of teenage and adult children; children up to the age of 12 years who are colonized; otherwise healthy children; healthy children known to have nasopharyngeal colonization; or children known to have an ear or pneumococcal infection. The metes and bounds of the claim are not understood.

(b) Claim 1 is further vague and indefinite, because lines 2 and 3 of the claim include the generic recitation: 'a kind of bacteria causative of human ear and respiratory infections'. The end of the claim however includes the narrower limitation: 'an ear and pneumococcal infection caused by the kind of bacteria'. The 'pneumococcal infection' recited herein is not limited to 'respiratory infections'. The scope of the claim is indeterminate. It is not clear whether the antigen is characteristic of pneumococci, or of any bacteria causative of human ear and respiratory tract infections.

(c) Claim 1 is indefinite in the recitation: 'substantially reduces' because it in unclear what is encompassed in the term 'substantially'. What degree of reduction qualifies as substantial reduction is not clear.

(d) Claim 1 is incorrect in the recitation: 'bacteria .... colonizes', as opposed to --bacteria ..... colonize--.

(e) Claim 3 is indefinite and/or lacks proper antecedence in the limitation: 'one of these bacteria'.

(f) Claims 4 and 7 are incorrect in the recitation 'bacteria is' as opposed to 'bacterium is' or 'bacteria are'.

(g) Claim 6 is indefinite in the limitation: 'the antibodies in each test are in part conjugated to a tag' and 'in part immovably fixed on a capture line'. It is unclear what is encompassed in 'antibodies ..... in part': a part of the same antibody conjugated to a tag, or some antibodies tagged and others not tagged?

(h) Claim 8 lacks antecedent basis in the limitation 'antibody' (see lines 4 and 5). Claim 8 depends from claim 6, which recited 'the antibodies'.

(i) Claims 2-8, which depend from clam 1, are also rejected as being indefinite, because of the indefiniteness identified above in the base claim.

Objection(s)

8) Claims 5 and 8 are objected to for the following reasons:

(a) Claim 5 is objected to for the recitation 'claim1'. It is suggested that Applicants replace the recitation with --claim 1--.

(b) Analogous criticism applies to claim 8 for the recitation '6mm' (see last line).

Remarks

9) Claims 1-8 stand rejected.

10) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

11) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available

through Private PAIR only. For more information about the PAIR system, see http://pair direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

12) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

July, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER